REMARKS

In view of the finality of this action, as indicated in the Examiner's Action of August 22, 2003, Applicant requests full reconsideration of this finality, namely making her action final and providing no opportunity to respond. Entry of Applicant's response on the record is entirely at the discretion of the Examiner. This is not appropriate in view of the continued inappropriate grounds of rejection. Applicant addressed all Examiner's prior action fully. The Examiner however continues to respectfully error in her assessment of the prior art. Applicant wishes to have the evidence of Dr. Lipp entered on the record in support of his arguments and rebuttal. Dr. Lipp's declaration is hereby incorporated by reference in its entirety to this response. Full reconsideration of the Examiner making her action of August 22, 2003 a Final Action and withdrawal of said finality is hereby requested.

Claims 1 to 18 now stand rejected under 35 U.S.C. 103(a) as being unpatentable over Gu et al (Pharm. Research, Vol. 7, No. 4, pgs 379-383, collectively, "Gu") in view of Harris et al (U.S. Patent No. 4,743,450, collectively, "Harris).

The Examiner incorrectly maintains that Gu et al renders obvious the process of making moexipril magnesium and that Gu discloses a process of making a moexipril alkaline salt by allegedly **reacting** moexipril hydrochloride with an alkaline stabilizing agent . Respectfully no such reaction is taught as supported by the Declaration of Dr. Lipp. The components are merely combined and any reaction is insignificant to the desired end result and clearly any such possible reaction that might occur is not a controlled reaction which is now included as a limitation of claim 1.

Referring now to the publication by Gu et al, "Drug-Excipient Incompatibility Studies of the Dipeptide Angiotensin Converting Enzyme Inhibitor, Moexipril Hydrochloride: Dry Powder vs Wet Granulation", Pharm Res.7(4):370-383, this publication discloses that moexipril hydrochloride can be stabilized by making compositions comprising moexipril hydrochloride and an alkaline stabilizing agent selected from sodium

bicarbonate, sodium carbonate and calcium carbonate. It is stated that the stabilization is accomplished only when the compositions are made by a wet granulation process. In the conclusion of the publication, it is postulated that the stabilization in part results from the neutralization of the acidic drug by the basic excipient at the outer surface of the granulated material. This was set out in the background of Applicant's disclosure. It is also stated in Gu that it is possible that a portion of the moexipril was converted to alkaline salts via granulation. It thus appears clear that Gu et at teaches that only a portion (if any) of the drug, and only that portion at the outer surface of the granules, may be converted to the alkaline salt, and **that the stable product thus results entirely or primarily not from conversion to alkaline salts, but from stabilization of the moexipril hydrochloride by the presence of the alkaline stabilizing compound in the final product.** Gu et al , discusses , the importance of stabilizing the product in order to avoid cyclization processes and how the stability varied with the pH values. For example, on page 381 at column 2, it was determined that with pH values below 4.5, a significant amount of degradation occurred. However at pH values between 4.5 and 10 the degradation rate was about 10 times slower. Gu also **postulates** only that the stabilization effect may be a result from the neutralization of the acid drug by basic excipients only at the outer surface of the granulated material. However, primarily the product is moexipril hydrochloride as the active. Gu et al is thus consistent with the teaching of U.S. Pat. No. 4,743,450, which, as set out below, teaches stable compositions comprising the unstable drug, stabilized by the presence of an alkaline compound in the final composition.

Contrary to the Examiner's alleged position Dr. Lipp states in Paragraph 4 of his Declaration,

> *"In my opinion, the inventions described in Claims 1 through 18 set out in the '173 patent application are **not** obvious in light of the teachings and disclosures of Gu et al. in view of Harris et al. I thus disagree with the conclusions reached by the Examiner in the Final Action with respect to the '173 patent application and these references".*

The Examiner is referred to Dr. Lipp's Declaration for a full analysis of his reasoning.

The claims are therefore not rendered obvious to one skilled in the art in view of Gu for the reasons provided by Dr. Lipp that Gu does not motivate one skilled in the art to manufacture moexipril magnesium from Gu's teaching of manufacturing moexipril

hydrochloride stabilized with an alkaline stabilizing agent. Nothing else might be inferred from the teachings of Gu et al and even if one were to read Gu et al in view of Harris, the resulting combination would not be more than, respectfully, merely the teachings of Gu or Harris.

The critical point is applicant has provided a process and product wherein not just "some" of the outer surface of particles of moexipril hydrochloride might be converted in a controlled manner to moexipril's magnesium salt in a random, unpredictable, uncontrolled manner, but that a substantial portion (at least 70%) is converted to moexipril's magnesium salt, by utilizing a sufficient amount of solvent so as to ensure such a reaction to take place.

As discussed by Dr. Lipp in item 7 of his declaration with respect to the Gu reference;

> *"such stabilizers are **not** conventionally taught or known to cause or participate in reactions in said formulations or to react with drugs such as ACE inhibitors during the processing of these formulations".*

Applicant previously submitted the Product Monograph for Univasc® (Moexipril Hydrochloride Tablets) hereby incorporated by reference wherein the tablets marketed by Schwarz Pharma (as listed in the FDA Orange Book as per the teachings of United States Patent No. 4,743,450) also hereby incorporated by reference, include magnesium oxide; unreacted but combined and functioning as a stabilizer. The Examiner is again referred to those pages. Full reconsideration is respectfully requested.

Dr. Lipp further states in paragraph 20 of his Declaration at the end thereof;

> *"Gu et al. does not teach or disclose a stabilizing reaction between moexipril hydrochloride and an alkaline compound that results in significant conversion of moexipril hydrochloride into a cation salt form such as moexipril sodium".*

Dr. Lipp concludes in paragraph 32 of his declaration;

> *"I disagree with the Examiner with respect to her assertion that Gu et al. teaches a process wherein moexipril hydrochloride is stabilized via a reaction with an alkaline stabilizing agent, such as sodium bicarbonate, sodium carbonate, and calcium carbonate. In addition, I disagree with the Examiner with respect to her comments concerning a lack of distinction between a reaction occurring between*

formulation components versus the mixing of formulation components. In particular, the Examiner states on page 6 of the Final Action that:

"The applicant's argument that a combination of ingredients rather than a reaction is taught is not persuasive. The term "reacting" is generic. One definition of "reacting" is the interchange of constituents with other substances. The mixing of the ingredients (as taught by Gu and Harris) constitutes this interchange."

"I disagree with the Examiner with respect to this point. With respect to the matter at hand, in my opinion, there is a clear distinction between a chemical reaction in which two compounds react chemically to produce two or more different compounds versus the physical mixing of formulation ingredients".

United States Patent No. 4,743,450 discloses a process for making the composition comprising quinapril hydrochloride stabilized by combining with an alkaline stabilizing agent. Clearly, there can be no reacting with this process but merely combining of ingredients. Example A refers to a wet granulation method for the manufacture of tablets from the listed materials including quinapril hydrochloride and magnesium carbonate in the amounts indicated which are not reacted but combined. The Examiner is referred to column 1, line 51 wherein it states, that an amount of a stabilizer compound suitable to retard cyclization, hydrolysis, and/or discoloration is contained in the pharmaceutical composition and that the composition is formed by the steps of **"contacting"** the drug with an amount of stabilizer suitable to retard cyclization and/or hydrolysis. It is also stated at the bottom of that column that the composition will also contain substances which do not interfere with the function of the stabilizing additives.

Referring to column 3, at line 25 of United States Patent No. 4,743,450, the use of the stabilizers is discussed extensively and the manner in which the cyclization and hydrolytic instability of the composition can be stabilized using a suitable quantity, i.e. an effective amount of an alkaline stabilizer. The amount utilized is any amount which will effectively retard or prevent degradation of the ACE inhibitor components. Further at the same column, discussing the saccharides which might be used, they are selected from substances which do not contain groups which could significantly interfere with the function of either the metal containing component or the drug component. **Further in relation to the**

excipients they are selected from those that do not interfere with the alkaline earth metal stabilizer's function in the composition. Dr. Lipp's evidence fully supports this position.

The essence therefore of that which is taught and claimed in United States Patent No. 4,743,450 is an ACE inhibitor which is susceptible to cyclization, hydrolysis, and discoloration, in combination with a suitable amount of an alkaline earth in the composition as a stabilizer. No where within the reference is there discussed any reactions, incorrectly concluded by the Examiner. Please see Dr. Lipp's comments in this regard. The reference is moot in this regard with the exception of contacting or combining the materials. For the composition to contain a stabilizer, clearly it must not have reacted with the drug, suitable saccharides or suitable excipients. United States Patent No. 4,743,450 merely teaches in Example A, at column 4, that the wet granulation method is used for the manufacture of 5 mg tablets. The reference is silent in relation to anything but the use of a more or less standard wet granulation process. There is no discussion as to how much wetting material should be used, other than Example C, wherein an amount of purified water is indicated but no use for that water is further discussed. Clearly therefore, it is impossible to conclude that United States Patent No. 4,743,450 discloses a process comprising the step of "reacting" since the magnesium compound must remain present in the final composition in order to fulfill its role as a stabilizer.

As evidence of this fact Dr. Lipp states in paragraph 34:

> *"Harris et al. teaches the use of alkaline magnesium compounds as conventional pharmaceutical stabilizers in formulations containing ACE inhibitors, which implies that these alkaline magnesium compounds act to inhibit reactions involving ACE inhibitor drugs in said formulations"*

and from paragraph 36:

> *"Thus, Harris et al. teach the use of alkaline and saccharide **stabilizers** in pharmaceutical formulations containing ACE inhibitor drugs. Pharmaceutical stabilizers are known in the art to be compounds that are added to pharmaceutical formulations for the purpose of inhibiting or preventing reactions involving drugs contained in said formulations from occurring".*

The Examiner is referred to these sections for Dr. Lipp's full analysis of the facts.

Clearly therefore one skilled in the art would not expect from a fair reading of Harris that any controlled reactions would take place between the ACE inhibitor and the alkaline compound to achieve at least 70% conversion since this would be contrary to the teachings of Harris as set out above. United States Patent No. 4,743,450 is silent with respect to any reaction as it is sought to stabilize the ACE inhibitor and that the stabilizing compound used must remain functional (not react) and not to be interfered with by any of the saccharides or excipients added to the composition. If it was expected from United States Patent No. 4,743,450 that the stabilizer would react then why would the above mentioned caution be set out clearly in the specification. Clearly, therefore the United States Patent No. 4,743,450 reference teaches combining or contacting but in no way discusses a reaction taking place, although the Examiner has respectfully mistakenly reached that conclusion. Please refer to the evidence of Dr. Lipp provided herewith for a full and correct analysis of the facts in this case.

In Applicant's process sufficient water is introduced (as a solvent) in the process to moisten and to thereby permit controlled a reaction to occur. There is no discussion or teaching in United States Patent No. 4,743,450 relating to this process. The Examiner may have incorrectly concluded that a reaction of quinapril and magnesium carbonate is inherent to the combination of the materials, **and incorrectly** that Harris discloses a process of making a solid pharmaceutical composition comprising quinapril magnesium when United States Patent No. 4,743,450 is entirely silent in this regard. Again the Examiner is referred to the enclosed declaration of Dr. Lipp for a correct analysis of the facts of this case.

Respectfully therefore, claims 1-18 of the present application cannot be refused as being obvious to one skilled in the art over Gu et al in view of United States Patent No. 4,743,450, since there is no motivation to react the ACE-inhibitor with the alkaline agent but merely to combine it so that the alkaline agents can act as stabilizers as set out above. Clearly nowhere within such a purported combination is there taught:

> *"A process of making a solid pharmaceutical composition comprising moexipril magnesium, said process comprising the step of reacting moexipril or an acid*

addition salt thereof with an alkaline magnesium compound in a controlled manner in the presence of a sufficient amount of solvent for a predetermined amount of time so as to convert at least 70% of the moexipril or moexipril acid addition salt to moexipril magnesium."

In support of this position in paragraph 17 Dr. Lipp states:

"I disagree with the Examiner with respect to her assertions concerning the teachings and disclosures of Gu et al. and Harris et al. As I describe further below, in my opinion, no combinations of the teachings and disclosures of these two references make obvious the inventions of the '173 patent application, including the combination of the teachings and disclosures of the Gu et al. reference in light of the teaching of an alkaline magnesium compound as a stabilizer for ACE inhibitor formulations in Harris et al. In particular, it is my opinion that the assertions made by the Examiner in the Final Action concerning the teachings and disclosures of Gu et al and Harris et al. and their relevance to the '173 patent application are incorrect for the following reasons, among others:

(i) Gu et al. does not teach or disclose a stabilizing reaction between moexipril hydrochloride and an alkaline compound that results in significant conversion of moexipril hydrochloride into a cation salt form such as moexipril sodium.

(ii) Gu et al. teaches that the use of an alkaline compound consisting of an inorganic salt of a Group II metal (calcium carbonate), similar to an alkaline magnesium compound, does not result in adequate stability.

(iii) Harris et al. teaches the use of alkaline magnesium compounds as conventional pharmaceutical stabilizers in formulations containing ACE inhibitors, which implies that these alkaline magnesium compounds act to inhibit reactions involving ACE inhibitor drugs in said formulations.

(iv) Harris et al. thus does not teach or disclose a stabilizing reaction between moexipril hydrochloride and an alkaline compound that results in significant conversion of moexipril hydrochloride into a cation salt form such as moexipril sodium.

(v) Harris et al. does not teach or claim that wet granulation processes or other processes involving the presence or use of water during formulation are an essential part of the invention.

(vi) Harris et al. teaches and claims that both alkaline and saccharide stabilizers are required to be present for the production of pharmaceutical dosage forms containing ACE inhibitors possessing adequate stability".

Clearly, a process of making a solid pharmaceutical composition comprising moexipril magnesium is taught by Applicant. Neither Gu et al or United States Patent No. 4,743,450 nor any combination of the teachings thereof teach such a process or the resulting composition . Moexipril magnesium is only a result of Applicant's process which includes the step of **reacting** (emphasis added) moexipril or an acid addition salt thereof with an alkaline magnesium compound in a controlled manner to convert at least 70% of the moexipril or acid addition salt thereof to moexipril magnesium. Applicant is not risking any unknown side reactions but is taking specific steps to provide specific desired results. To do so a solvent must be present in order for the reaction to occur, and the solvent must be present in an amount so as to convert at least 70% of the moexipril or moexipril acid addition salt to moexipril magnesium. This simply is not taught directly or indirectly in Gu et al or United States Patent No. 4,743,450 and further in any combinations thereof. There is no discussion whatsoever of the conversion at least 70% of the moexipril or moexipril acid addition salt to moexipril magnesium as a solid pharmaceutical composition in any of the references cited herein by the U.S. Examiner.

A reaction is not disclosed, inferred, suggested or discussed in Harris whatsoever. In fact only the stabilizing activity of the magnesium compound is discussed and the importance of avoiding excipients and saccharides which might interfere with that stabilizing function. Gu et al postulates that a minor insignificant portion may react but the

stabilization is a result of the combination of the moexipril hydrochloride with the alkaline stabilizer as evidenced by the Product Monograph previously provided. No other conclusion can be reached.

Dr. Lipp further also states in his declaration in paragraph 18:

> *"Further, it is also my opinion that the Gu et al. and Harris et al. references in part both in teach away from each other and teach away from the inventions of the '173 patent application".*

Clearly all claims depend from Claim 1 except claim 14. How therefore could claims 1-13 and 15-18 lack an inventive step if Claim 1 is in fact inventive over Gu et al in view of Harris which Applicant and Dr. Lipp have correctly concluded and argued, in spite of the assertions of the Examiner. Claims 2-13 and 15-18 refers to the compound further comprise additional limiting steps of adding the moexipril or acid addition salt thereof and the alkaline magnesium compound to the solvent and mixing in the liquid state and subsequently evaporating the solvent to obtain a dried material and further processing the dry material into a solid pharmaceutical composition. For the same reasons therefore set out in relation to Claim 1, Claims 2-13 and 15-18 would therefore be novel and non-obvious. Claim 14 is also novel and non-obvious since neither Gu nor Harris teach a solid composition containing moexipril wherein at least 70% of the moexipril present is moexipril magnesium.

No reference is made to moexipril magnesium in United States Patent No. 4,743,450. None of the teachings discuss or even infer the compound moexipril magnesium in that the final compound quinapril magnesium does not necessarily require a stabilizer as set out in the teachings of Applicant's invention. However, United States Patent No. 4,743,450 includes a stabilizer; Applicant's compound does not.

All the dependent claims are therefore inventive in view of the argument set out above since none of Gu et al alone or in any combination with United States Patent No. 4,743,450 teaches the invention, moexipril magnesium.

Dr. Lipp clearly states in paragraph 27 in relation to the evidence provided as Exhibit B of his declaration:

"Thus, this standard reference teaches that the purpose of a granulating liquid is to cause granules or particles of drugs and excipients to adhere to each other, not to dissolve and to react with each other (i.e., the binding liquid is described to coat and bind the particles, not to dissolve them). Similarly, when discussing the advantages of wet granulation, it is stated on pages 114 and 115 of this reference that:

"The purpose of granulation is to enlarge the particle size of a powder and obtain uniform particles which will flow readily through the tablet machine hopper and feed frames into the dies. This results in a number of improvements in the properties of the powder with regards to tableting".

The Examiner is again referred to Dr. Lipp's Declaration.

Referring to the traditional test enunciated in Graham vs. John Deere Company 383 U.S. 1, 148 U.S.P.Q. 459 1966, Applicant has followed the Section 103 nonobviousness requirement set out therein the scope and content of Gu et al and Harris has been determined as evidenced by Dr. Lipp's Declaration, and the differences between the prior art and the claims at issue have been ascertained. The patentability of the claims at hand stem from the fact that the specific combination of the claimed elements was not disclosed in Gu et al or Harris or any combinations thereof and the specific combination of claimed elements was nonobvious to one of ordinary skill in the art.

As supported by the evidence of Dr. Lipp there is no motivation within Gu et al or Harris or Gu et al in view of Harris to arrive at Applicant's amended claim set. Though moexipril hydrochloride and magnesium carbonate are capable of an acid-base reaction, it is difficult to control their process so as to completely avoid an acid-base reaction in the making of their stabilized composition. The exact composition of the final product of Gu is thus uncertain and probably variable, if the teaching of Gu et al in view of U.S. Pat. No. 4,743,450 is followed. No motivation however from either reference to do so is present from a fair reading of either reference. Full reconsideration is respectfully requested.

Dr. Lipp concludes in paragraph 28:

*"In my opinion, such information would **not** teach a skilled formulator that a wet granulation process can allow for a significant amount of reaction to occur between granular formulation components initially present in a dry state as part of a powder mix before the liquid of granulation is added, as is the process described in the Gu et al. reference. The combining of solid granules of drugs and excipients in a wet granulation process is very different than a reaction occurring between solubilized drug and excipient components in an equilibrium solution".*

Clearly, the prior art does not suggest or provide any reason or motivation to make such a modification as purported by the Examiner. With reference to In Re: Regal, 526 F. 2d 1399, 1403 n. 6, 188 USPQ 136, 139 n. 6 (CCPA 1975).

> "There must be some logical reason apparent from positive, concrete evidence of record which justifies a combination of primary and secondary references".

In Re: Geiger, 815 F. 2d 686, 688, 2 USPQ 2d 1276, 1278 (Fed. Cir. 1987) (obviousness can not be established by combining pieces of prior art absence some "teachings, suggestion, or incentive supporting the combination"): In Re: Cho. 813 F. 2d 378, 382, 1 USPQ 2d 1662, 1664 (Fed. Cir. 1987)("discussing the Board's holding that the artisan would have been motivated to combine the references").

Therefore, it Applicant's view there is no evidence of motivation in the prior art, either within the references themselves, or knowledge generally available to one of ordinary skill in the art, to make the purported changes suggested by the Examiner to arrive at the claimed subject matter. Respectfully, the Examiner is creating a 20/20 hindsight reconstruction using Applicant's invention as a blue print to allegedly find elements of Applicant's combination in the prior art. This is not permissible as set out below.

Even if one skilled in the art were to combine Gu et al with Harris they would arrive at moexipril hydrochloride which is stabilized by an alkaline agent and preferably magnesium oxide as per the product monograph of the moexipril hydrochloride tablets manufactured by Schwarz Pharma attached in the prior Information Disclosure Statement

provided. Applicant is not "combining" but is "reacting" the active and the agents to result in the moexipril magnesium.

Dr. Lipp states in paragraph 31:

> *"Gu et al. only refer to the possibility of a portion of the moexipril hydrochloride converting to the cation salt; it is not taught that such a reaction, if it occurs at all, occurs to an appreciable extent".*

In fact it is well established that for a combination of references to render an invention obvious, it must be obvious that the references can be combined; In Re Avery 186 U.S.P.Q.161 (CCPA 1975). The references themselves and not in retrospect, must suggest what has to be done. In Re: Skoll 187 USPQ 481 (CCPA 1975). There must be some reason for the combination other than hindsight gleaned from their invention itself. Interconnect Planning Corp., vs. Feil, 774 F. 2d 1132, 1134 (Fed. Cir. 1985). See also Panduit Corp. vs. Dennision Mfg. & Co., 810 F. 2d 1561, 1568 (Fed. Cir. 1988) where the court said:

> "Elements of separate prior art patents cannot be combined when there is no suggestion of such combination anywhere in those patents".

Although the Examiner suggests that the structure could readily be modified to form a combination of the claims at issue, the mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification. Please See in Re: Gordon 733 F. 2d 900-902, 221 USPQ 1125, 1127 (Fed. Cir. 1984); In Re: Grabiak, 769 F. 2d 729, 731, 226 USPQ 870, 872 (Fed. Cir. 1985).

In Re: Fritch, 23 U.S.P.Q. 2d 1780 (Fed. Cir. 1992)

> *"Wilson and Hendrix fail to suggest any motivation for, or desirability of, the changes espoused by the Examiner and endorsed by the Board. Here, the Examiner relied upon hindsight to arrive at the determination of obviousness. It is impermissible to use the claimed invention as an instruction manual or "template" to piece together the teachings of the prior art so that the claimed invention is rendered obvious. The court has previously stated that "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."*

Clearly there is no motivation within Gu et al to modify his composition into Applicant's process absent some teaching in Gu et al to do so with or without the teachings of Harris, which is simply not the case.

Dr. Lipp concludes in paragraph 46:

> *"Thus, in my opinion, neither of the references Gu et al. and Harris et al. make obvious the inventions of the '173 patent application. As I described above, neither of these references teaches or makes obvious a process for the conversion of moexipril hydrochloride to moexipril magnesium via a reaction with an alkaline magnesium compound for the purpose of increased stability. Additionally, it is also my opinion that these two references in part both teach away from each other and teach away from the inventions of the '173 patent application. I thus disagree with the assertion made by the Examiner with respect to the combined teachings of these references"*

and from paragraph 47:

> *"However, in addition to the reasons that I described above with respect to the these references considered individually, it is my also opinion that the Examiner is incorrect in asserting that these references can be read together in the manner the Examiner describes above (i.e., utilizing Harris et al. to teach the use of an alkaline magnesium compound in the processes described in Gu et al.). For example, as I described in Paragraph 33 above, Gu et al. teaches away from the use of Group II alkaline salt compounds such as alkaline calcium or alkaline magnesium compounds. In contrast, Harris et al. teaches the preferred use of an alkaline magnesium compound. Additionally, Gu et al. teaches that the use of a wet granulation process is required to obtain suitable formulation stability. In contrast, Harris et al teaches that a variety of formulation methods and pharmaceutical dosage forms can be utilized in practicing the inventions disclosed therein".*

Hindsight is not appropriate when considering the claim set of Applicant, as set out below!

ATD Corporation v. Lydall, Inc., 48 USPQ 2d 1321, 1329 (Fed. Cir. 1998)

Determination of obviousness can not be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention. **There must be a teaching or suggestion within the prior art, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources of information, to select particular elements, and to combine them in the way they were combined by the inventor.(emphasis added)**

In re Oetiker, 24 USPQ 2d 1443, 1446 (Fed. Cir. 1992)

The combination of elements from non-analogous sources, in a manner that reconstructs the applicant's invention only with the benefit of hindsight, is insufficient to present a prima facie case of obviousness. **There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the combination.** (emphasis added)That knowledge can not come from the applicant's invention itself.

Dr. Lipp therefore concludes in paragraph 48:

"In summary, it is my opinion that the inventions disclosed in the '173 patent application are not made obvious by any combination of the teachings and disclosures of Gu et al. and Harris et al. Both Gu et al and Harris et al. disclose processes for the stabilization of various ACE inhibitors and their acid addition salts, including moexipril hydrochloride, via the production of formulations containing these ACE inhibitors in their original forms (i.e., in the form of moexipril hydrochloride for Gu et al. and quinapril hydrochloride in Harris et al.) in combination with one or more pharmaceutical stabilizers such as alkaline compounds. In contrast, the '173 patent application discloses novel formulations

and processes for the stabilization of moexipril hydrochloride via its conversion into the form of moexipril magnesium".

Full reconsideration is therefore respectfully requested, and the entry of this rebuttal including the Declaration of Dr. Lipp is earnestly solicited.

Should the Examiner have any questions she is respectfully requested to contact Neil H. Hughes at (905) 771-6414 at his/her convenience.

Respectfully submitted,

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Agent for the Applicant

NHH:jlh
Enclosures